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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/018,773	03/22/2002	Arnold Hilgers	Q67842	1749

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EXAMINER	
NGUYEN, DAVE TRONG	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 09/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/018,773	HILGERS, ARNOLD	
	Examiner	Art Unit	
	Dave T Nguyen	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 June 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *61-73,78-89 and 95-100* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *61* is/are allowed.

6)☒ Claim(s) *62-73, 78-89, and 95-100* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on June 23, 2004 has been entered.

Claims 61-68, 71, 72, 80 have been amended, and claims 74-77, 90-94 have been canceled by the amendment dated June 23, 2004.

Claims 61-73, 78-89, and 95-100, to which the following grounds of rejection remain and/or are applicable, are pending.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 62-71, 73, 78-89, 95-98 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation of "A method according to claim" or "A composition according to claim" in dependent Claims 62-71, 73, 78-89, 95-98 is indefinite because all of the base claims from which the claims depend are clearly drawn one specifically disclosed method or composition. As such, the recitation of "A" is non-specific, and thus, does not

appear to clearly specify as to what are exactly the metes and bounds of the method intended for claiming as a whole in each of the dependent claims. A simple change from "A" to -- The -- would obviate the rejection.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 72-73, 78-89, 95-100 are rejected under 35 USC 102 (b) as being anticipated by any of Woiszvillo (US Pat No. 5,849,884), OctoPlus (EP 0 842 657), or Magnus (EP 0 213 303).

The claims claim a composition comprising microparticles produced by the claimed methods, wherein the limitation of "composed of at least 75% of said polymer compounds and 25% or less of said biological material in said aqueous solution" only can be characterized or made meaningful when the composition are interpreted as product by process claims. All dependent claims are interpreted as the composition according to the base claims. The fact that 75% of polymers used as starting materials in Applicant's claimed method are now in the microparticle forms of the claimed

compositions does not necessarily particularly point out as to what is exactly the final concentration or weight of the polymer or microparticle relative to that of the biological material present physically in the claimed compositions. Thus, to the extent that the total weight of the claimed composition are not limited in any way to any concentration and/or weight of either the microparticle or biological material, the newly added limitation does not carry any patentable weight for the claimed compositions. As such, the prior art rejections remain applicable as stated here below:

With respect to the composition claimed as set forth in the immediately preceding paragraphs, Woiszvillo teaches the same on column 3, line 21 –column 4, line 5, examples). OctoPlus teaches the same on pages 3-5. Particularly, OctoPlus teaches on page 4, lines 39-41, that suitable emulsifiers are copolymers, preferably block-copolymers, of units of the two incompatible polymers, e.g., a block-copolymer of PEG and Dextran, used to create the two-phase system. Magnus also teaches the same throughout the disclosure, particularly pages 2-4, 5-6, and 12. With respect to Woiszvillo: column 3 discloses that the polymers are carbohydrate based polymers, dextran or a polymer mixture of polyminylpyrrolidone and polyethylene glycol (PEG); The MW of PEG is disclosed on column 12; Example 5, column 19 discloses that polylysine is employed as a nucleic acid binding agent; Column 10 discloses that surfactant composed of any known phospholipid can be employed for attachment to the surface of the formed microparticles; and MW of Dextran is disclosed on column 22. With respect to Magnus, Magnus teaches that PEG and dextran can be used in a two-phase system, wherein MW of both are also disclosed, page 5; page 3 discloses that

one way to achieve removal of water from the dispersed phase comprises the application of methods such as evaporation; Page 12 of Magnus also discloses that particles can be produced without heating, if the dispersed phase is dehydrated with a watermiscible solvent.

The functional limitations of an occurrence of a spontaneous formation of the dispersed phase, and of the percent relative to that used as starting materials in Applicant's claimed process do not carry any patentable weight, since the office does not have the facilities for examining and comparing applicant's product with the product of the prior art in order to establish that the product of the prior art does not possess the same functional characteristics of the claimed product. In the absence of factual evidence to the contrary, the burden is upon the applicant to prove that the claimed products are **functionally different** than those taught by the prior art and to establish patentable differences. See *Ex parte Phillips,* 28 USPQ 1302, 1303 (BPAI 1993), *In re Best,* 562, F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte Gray,* 10 USPQ2d 1922, 1923 (BPAI 1989). Again, the claiming of a new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. *In re Best*, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977); *In re Spada,* 15 USPQ2d 1655, Federal Circuit, 1990. See also MPEP § 2112.01 with regard to inherency and product-by-process claims.

Furthermore, the skill of a person skilled in the art of making microparticles is relatively high, as evidenced by the totality of the prior art of record, and as such, it is well-recognized in the prior art that aqueous solutions of two incompatible polymers will

spontaneously separate into a dispersed and continuous phase when a critical polymer concentration has been reached, *e.g.,* evaporation of water. In fact, Woiszvillo teaches on column 12, last paragraph, that "the microparticles may be formed at lower temperatures by utilizing a higher macromolecule concentration". On the other hand, when two incompatible polymers are mixed in such a way that the concentration in the final mixture is already above the critical concentration (see column 7, especially lines 32-40), mechanical energy (e.g., vortexing, stirring) should be put in the system in order to get a finely dispersed phase. Note also that although Woiszvillo teaches the use of conventional emulsification means, like stirring, vortexing and sonication, evaporation must be necessarily present in the energy added steps, particularly in view of the presence of the added energy as the result of the use of emulsification means, like stirring, vortexing and sonication. As such, a spontaneous formation of a dispersed phase is not excluded. Furthermore, the formation of microparticles can also be observed just by heating one-phase aqueous solutions of incompatible polymers, *e.g.,* example 14.

Thus, the claims are anticipated by the cited references.

Note also that it is well recognized by a person of ordinary skill in the art, as evidenced by the totality of the prior art of record, that a dispersed phase would form when a critical polymer concentration has been reached, and that it is within the purview of those of ordinary skill in the art of making microparticles to employ any concentration step such as evaporation without heating in order to achieve the critical polymer concentration required for the formation of a dispersed phase in a two-phase system

comprising to incompatible polymers such as dextran and PEG, and a biologically active material such as a nucleic acid molecule.

Claims 72-73, 78-89, 95-100 are rejected under 35 USC 103(a) as being unpatentable over OctoPlus (EP 0 842 657), or Magnus (EP 0 213 303), each of which taken with Carli (US Pat No. 6,355,273), Mathiowitz (US Pat No. 6,745,779 B2), Burke (US Pat No. 6,183,781) or Gombotz (US Pat No. 6,274,175).

The rejections of the claimed composition as being anticipated by OctoPlus (EP 0 842 657), or Magnus (EP 0 213 303) remain applicable as indicated above. To the extent that the claimed composition embrace a particular weight of microparticle and biological material present in the composition, the claims are also obvious under 35 USC 103:

More specifically, Carli (US Pat No. 6,355,273), Mathiowitz (US Pat No. 6,745,779 B2), Burke (US Pat No. 6,183,781) or Gombotz (US Pat No. 6,274,175) all teach that it is well accepted within the scientific community to employ any percent weight of the microparticle and biological material for the delivery of the biological material to a target tissue or cell. For example, Carli teaches on column 10 that the obtained microparticles has 92.15% by weight of the product, and the drug (nicardipine) has 22.5% by weight of the formed product. Mathiowitz teaches and claim on column 16 that the weight of the biological material of DNA, which can be formulated or loaded into the polymeric microparticle, is about 0.1-90%. Burke teaches on column 14 that formulated microparticles can contain a peptide as the biological material in an amount

from at least 0.1 preferably 0.5 to 20% by weight relative to the (co)-polymer matrix, preferably 2.0 to 10, especially 3 to 6% of weight. Gombotz teaches on column 9 that the range of loading of the GM-CSF as the biological material to be delivered is typically between about 0.001% and 10 %, by weight....In a preferred embodiment, GM-CSF is incorporated into PLGA blends to 2% by weight.

Thus, it would have been obvious for a skilled artisan as a matter of design choice to incorporate and/or modify the percent weight of the microparticles and biological material in the methods employed in the primary references, depending on a particular nature of usage of the delivered biological material. One of ordinary skill in the art would have been motivated to do so because the cited prior art teaches that the percent weight of microparticles and biological materials can be routinely modified and because Carli, Mathiowitz, Burke, and Gombotz all teach that it is well accepted within the scientific community to employ any percent weight of the microparticle and biological material for the delivery of the biological material to a target tissue or cell.

Thus, the claimed invention as a whole, was *prima facie* obvious.

The following references are cited to further show that it is well recognized by a person of ordinary skill in the art that a dispersed phase would form when a critical polymer concentration has been reached, and that it is within the purview of those of ordinary skill in the art of making microparticles to employ any concentration step such as evaporation without heating in order to achieve the critical polymer concentration required for the formation of a dispersed phase in a two-phase system comprising to

incompatible polymers such as dextran and PEG: Orly, US Pat No. 5,672,301, Gibson, US 6,291,013, Hennink, US 6,303,148 and US 6,395,302.

Applicant's response (pages 9-11) has been considered by the examiner but is not found persuasive because of the reasons set forth above. More specifically, applicant's attempt to assert that since the methods as claimed are novel, the claimed compositions, which are claimed in the form of a product by process claim, are also free of the prior art of record, and thus, are patentable. However, the issue is not that the examiner questions the patentability of the method according to claim 61 but rather is that the compositions as claimed do not distinguish themselves in any way structurally to that of the prior art of record, particularly in the absence of any factual evidence on record. As such, the claimed compositions remain properly rejected over the prior art of record.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner *Dave Nguyen* whose telephone number is **571-272-0731**.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, *Amy Nelson*, may be reached at **571-272-0804.**

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center number, which is **703-872-9306.**

Any inquiry of a general nature or relating to the status of this application should be directed to the *Group receptionist* whose telephone number is **(703) 308-0196**.

Dave Nguyen
Primary Examiner
Art Unit: 1632

DAVE T. NGUYEN
PRIMARY EXAMINER

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